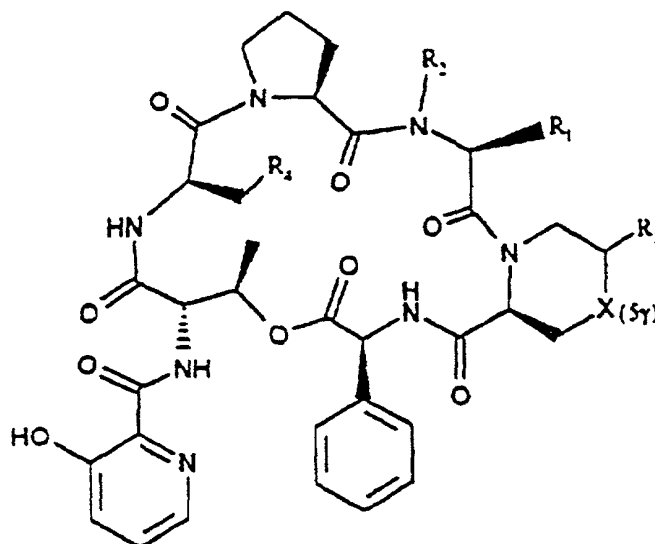


CLAIMS

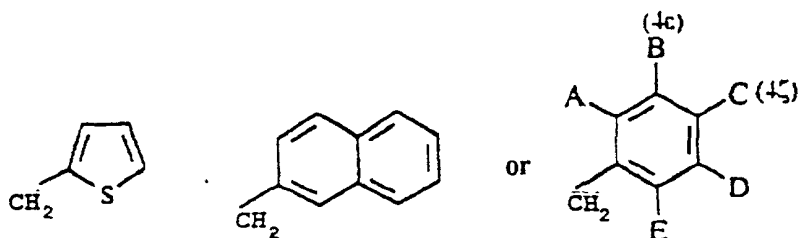
1. Compound characterized in that it is represented by the general formula I



I

in which:

- 5                   - R<sub>2</sub> and R<sub>4</sub> represent, independently of each other, a hydrogen atom or a methyl group,
- R<sub>3</sub> represents a hydrogen atom or a hydroxyl group,
- X represents a CO, CHOH or CH<sub>2</sub> group, and
- 10                  - R<sub>1</sub> represents:



with

- for the meta derivatives:

A, C, D and E representing a hydrogen atom, and

B being able to represent:

- a halogen, and preferably a fluorine atom,
  - 5        - a monoalkylamino or dialkylamino group,
- with alkyl preferably representing a methyl or ethyl group,

- an ether group,
- a thioether group,
- 10       - a C<sub>1</sub> to C<sub>3</sub> alkyl group, or
- a trihalogenomethyl group, preferably trifluoromethyl.

- for the para derivatives:

A, B, D and E representing a hydrogen atom, and

15       C being able to represent:

- a halogen,
- an NR<sub>1</sub>R<sub>2</sub> group with R<sub>1</sub> and R<sub>2</sub> representing, independently of each other, a group selected from among
- 20       - hydrogen,
- a straight-chain or branched C<sub>1</sub> to C<sub>4</sub> alkyl group where, when one of the substituents R<sub>1</sub> or R<sub>2</sub> represents a methyl group, the other necessarily represents an ethyl group,
- 25       - an alkyl-cycloalkylmethyl group with a C<sub>3</sub> to C<sub>4</sub> cycloalkyl,
- an optionally substituted C<sub>3</sub> to C<sub>4</sub> cycloalkyl group,

- a straight-chain or branched  $C_1$  to  $C_4$  alkenyl group where, when one of the substituents  $R_1$  or  $R_2$  represents an alkenyl group, the other is different from a methyl group or a  $C_3$  to  $C_6$  cycloalkyl group,

5                   - a substituted or unsubstituted N-pyrrolidinyl group,

- an ether group,

- a thioether group,

- an acyl or alkoxycarbonyl group,

10                   - a  $C_1$  to  $C_4$  alkyl group which is straight-chain or branched and which is preferably selected from among the methyl, isopropyl and tert-butyl groups,

- an alkylthiomethyl group,

- an aryl group, preferably a phenyl group,

15           or

- a trihalogenomethyl group, preferably trifluoromethyl and

- for the meta-para disubstituted derivatives:

A, D and E representing a hydrogen atom, and

20   B being able to represent:

- a halogen, preferably a fluorine atom,

- a monoalkylamino or dialkylamino group with alkyl preferably representing a methyl or ethyl group,

- an ether group,

25                   - a thioether group,

- a  $C_1$  to  $C_4$  alkyl group, and

C being able to represent:

- a halogen, and preferably a fluorine atom,

- an amino, monoalkylamino or dialkylamino group with alkyl preferably representing a methyl group with the proviso that B is different from a bromine or chlorine atom, or a substituted or unsubstituted allyl group,

- an ether group,
- a thioether group,
- a C<sub>1</sub> to C<sub>6</sub> alkyl group, or
- a trihalogenomethyl group, preferably

10 trifluoromethyl, and

- for the ortho-para disubstituted derivatives:

B, E and D representing a hydrogen atom and A and C a methyl group.

2. Compound according to claim 1,  
15 characterized in that it is preferably:

4 $\zeta$ -methylthio-

de(4 $\zeta$ -dimethylamino)pristinamycin I<sub>A</sub>,

4 $\zeta$ -methylthio-

de(4 $\zeta$ -dimethylamino)pristinamycin I<sub>B</sub>,

20 5 $\gamma$ -hydroxy-4 $\zeta$ -methylthio-

de(4 $\zeta$ -dimethylamino)pristinamycin I<sub>B</sub>,

4 $\zeta$ -methyl-de(4 $\zeta$ -dimethylamino)pristinamycin

I<sub>A</sub>,

4 $\zeta$ -methyl-de(4 $\zeta$ -dimethylamino)pristinamycin

25 I<sub>B</sub>,

4 $\zeta$ -methoxy-de(4 $\zeta$ -dimethylamino)pristinamycin

I<sub>A</sub>,

4 $\zeta$ -methoxycarbonyl-

- de(4 $\zeta$ -dimethylamino)pristinamycin I<sub>A</sub>,  
 4 $\zeta$ -chloro-de(4 $\zeta$ -dimethylamino)pristinamycin  
 I<sub>A</sub>,  
 4 $\zeta$ -bromo-de(4 $\zeta$ -dimethylamino)pristinamycin I<sub>A</sub>,  
 5 4 $\zeta$ -bromo-de(4 $\zeta$ -dimethylamino)pristinamycin I<sub>H</sub>,  
 4 $\zeta$ -iodo-de(4 $\zeta$ -dimethylamino)pristinamycin I<sub>A</sub>,  
 4 $\zeta$ -iodo-de(4 $\zeta$ -dimethylamino)pristinamycin I<sub>H</sub>,  
 4 $\zeta$ -trifluoromethyl-de(4 $\zeta$ -dimethylamino) -  
 pristinamycin I<sub>A</sub>,  
 10 4 $\zeta$ -trifluoromethyl-de(4 $\zeta$ -dimethylamino) -  
 pristinamycin I<sub>H</sub>,  
 4 $\zeta$ -tert-butyl-de(4 $\zeta$ -dimethylamino) -  
 pristinamycin I<sub>A</sub>,  
 4 $\zeta$ -isopropyl-de(4 $\zeta$ -dimethylamino) -  
 15 pristinamycin I<sub>A</sub>,  
 4 $\zeta$ -isopropyl-de(4 $\zeta$ -dimethylamino) -  
 pristinamycin I<sub>H</sub>,  
 4 $\epsilon$ -methylamino-de(4 $\zeta$ -dimethylamino) -  
 pristinamycin I<sub>A</sub>,  
 20 4 $\epsilon$ -methoxy-de(4 $\zeta$ -dimethylamino)pristinamycin  
 I<sub>A</sub>,  
 4 $\epsilon$ -methoxy-de(4 $\zeta$ -dimethylamino)pristinamycin  
 I<sub>H</sub>,  
 4 $\epsilon$ -fluoro 4 $\zeta$ -methyl-de(4 $\zeta$ -dimethylamino) -  
 25 pristinamycin I<sub>A</sub>,  
 4 $\zeta$ -amino-de(4 $\zeta$ -dimethylamino)pristinamycin  
 I<sub>A</sub>,  
 4 $\zeta$ -ethylamino-de(4 $\zeta$ -dimethylamino) -

- pristinamycin I<sub>A</sub>,  
 4ζ-diethylamino-de(4ζ-dimethylamino) -  
 pristinamycin I<sub>A</sub>,  
 4ζ-allylamino-de(4ζ-dimethylamino) -
- 5 pristinamycin I<sub>A</sub>,  
 4ζ-diallylamino-de(4ζ-dimethylamino) -  
 pristinamycin I<sub>A</sub>,  
 4ζ-allylethylamino-de(4ζ-dimethylamino) -  
 pristinamycin I<sub>A</sub>,  
 4ζ-ethylpropylamino-de(4ζ-dimethylamino) -
- 10 pristinamycin I<sub>A</sub>,  
 4ζ-ethylisopropylamino-de(4ζ-dimethylamino) -  
 pristinamycin I<sub>A</sub>,  
 4ζ-ethylmethylcyclopropylamino-  
 15 de(4ζ-dimethylamino)pristinamycin I<sub>A</sub>,  
 4ζ-(1-pyrrolidinyl) -de(4ζ-dimethylamino) -  
 pristinamycin I<sub>A</sub>,  
 4ζ-trifluoromethoxy-de(4ζ-dimethylamino) -  
 pristinamycin I<sub>A</sub>,
- 20 4ζ-allyloxy-de(4ζ-dimethylamino)pristinamycin  
 I<sub>A</sub>,  
 4ζ-ethoxy-de(4ζ-dimethylamino)pristinamycin  
 I<sub>A</sub>,  
 4ζ-ethylthio-de(4ζ-dimethylamino) -
- 25 pristinamycin I<sub>A</sub>,  
 4ζ-methylthiomethyl-de(4ζ-dimethylamino) -  
 pristinamycin I<sub>A</sub>,  
 4ζ-(2-chloroethoxy) -de(4ζ-dimethylamino) -

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characterized in that the gene(s) whose expression is altered is/are selected from among the genes which are involved in the biosynthesis of L-2-aminobutyric acid, 4-dimethylamino-L-phenylalanine (DMPAPA), L-pipecolic acid, L-phenylglycine and/or 3-hydroxypicolinic acid.

6. Process according to claim 4 or 5, characterized in that at least one of the genes is selected from among the papA, papM, papC (SEQ ID No. 2), papB (SEQ ID No. 3), pipA (SEQ ID No. 5), snbF (SEQ ID No. 6) and hpaA (SEQ ID No. 8) genes.

7. Process according to one of claims 3 to 6, characterized in that the said genetic modification renders at least one of the genes involved in the biosynthesis of the group B streptogramin precursors partially or totally incapable of encoding the natural enzyme.

8. Process according to one of claims 3 to 7, characterized in that the genetic modification consists of a disruption of one of the genes involved in the biosynthesis of the group B streptogramin precursors.

9. Process according to one of the preceding claims, characterized in that the mutant strain employed is derived from the strain S. pristinaespiralis and preferably from the strain S. pristinaespiralis SP92.

10. Process according to claim 9, characterized in that the strain is preferably the



strain SP92:pVRC508.

11. Process according to claim 9, characterized in that the strain is preferably the strain SP212.

5 12. Process according to claim 9, characterized in that the strain is preferably the strain SP92pipA::Qam<sup>R</sup>.

13. Process according to claim 9, characterized in that the strain is preferably the  
10 strain SP92hpA::Qam<sup>R</sup>.

14. Process according to any one of the preceding claims, characterized in that the novel precursor, which is introduced into the culture medium, is selected from among derivatives or analogues of  
15 amino acids and alpha-ketocarboxylic acids.

15. Process according to any one of the preceding claims, characterized in that the novel precursor is preferably selected such that it is related to the precursor whose biosynthesis is altered.

20 16. Process according to claim 14 or 15, characterized in that the novel precursor is preferably a derivative of phenylalanine when the gene whose expression is altered relates to the biosynthesis of DMPAPA.

25 17. Process according to one of the preceding claims which is useful for preparing pristinamycin IB.

18. Nucleotide sequence, characterized in

that it is selected from among:

(a) all or part of the genes papC (SEQ ID No. 2), papB (SEQ ID No. 3), pipA (SEQ ID No. 5), snbF (SEQ ID No. 6) and hpaA (SEQ ID No. 8),

5 (b) sequences which hybridize with all or part of the (a) genes, and

(c) sequences which are derived from (a) and (b) sequences on account of the degeneracy of the genetic code.

10 19. Nucleotide sequence according to claim 18, characterized in that it is selected from among the papC (SEQ ID No. 2), papB (SEQ ID No. 3), pipA (SEQ ID No. 5), snbF (SEQ ID No. 6) and hpaA (SEQ ID No. 8) genes.

15 20. Recombinant DNA encompassing a gene selected from among the papC (SEQ ID No. 2), papB (SEQ ID No. 3), pipA (SEQ ID No. 5), snbF (SEQ ID No. 6) and hpaA (SEQ ID No. 8) genes.

20 21. Vector, characterized in that it encompasses a nucleotide sequence according to claim 18 or 19 or a recombinant DNA according to claim 20.

22. Use of a sequence according to claim 18 or 19 and/or of a vector according to claim 21 for preparing metabolites.

25 23. Polypeptide which results from the expression of a sequence according to claim 18 or 19.

24. Mutant S. pristinaespiralis strain, characterized in that it possesses at least one genetic

modification within one of its papC (SEQ ID No. 2),  
papB (SEQ ID No. 3), pipA (SEQ ID No. 5), snbF (SEQ ID  
 No. 6) and/or hpaA (SEQ ID No. 8) genes.

25. Mutant strain according to claim 24,  
 5 characterized in that it is the strain SP92pipA::Ωam<sup>R</sup>.

26. Mutant strain according to claim 24,  
 characterized in that it is the strain SP92hpaA::Ωam<sup>R</sup>.

27. Mutant S. pristinaespiralis strain,  
 characterized in that it possesses a genetic  
 10 modification which consists of a disruption of the papA  
 gene by double homologous recombination, such as SP212.

28. Compound, characterized in that it is  
 4-trifluoromethoxyphenylalanine,  
 3-methylaminophenylalanine, 3-methylthiophenylalanine,  
 15 3-fluoro-4-methylphenylalanine,  
 4-methylaminophenylpyruvic acid, 3-ethoxyphenylalanine,  
 4-allylaminophenylalanine, 4-diallylaminophenylalanine,  
 4-allylethylaminophenylalanine,  
 4-ethylpropylaminophenylalanine,  
 20 4-ethylisopropylaminophenylalanine,  
 4-ethylmethylcyclopropylaminophenylalanine,  
 4-(1-pyrrolidinyl)phenylalanine,  
 4-ethylthiomethylphenylalanine,  
 4-O-(2-chloroethyl)tyrosine,  
 25 3-dimethylaminophenylalanine and  
 3-ethylaminophenylalanine

29. Pharmaceutical composition,  
 characterized in that it contains at least one compound

[illegible]